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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/561,115	12/15/2005	Norikazu Ohtake	BY0026	1781

210 7590 07/11/2007

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EXAMINER	
JARRELL, NOBLE E	
ART UNIT	**PAPER NUMBER**
1624	
MAIL DATE	**DELIVERY MODE**
07/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/561,115	OHTAKE ET AL.	
	Examiner	Art Unit	
	Noble Jarrell	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-25 and 30-33* is/are rejected.

7)☒ Claim(s) *26-29* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/15/2005*.
4) ☑ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I in the reply filed on 6/7/2007 is acknowledged. The election of example 1 on page 73 of the specification is also acknowledged.

Specification

2. The abstract of the disclosure is objected to because example 1 (page 73) is misnamed (pyridine should be pyrimidine). Applicants are invited to correct any other nomenclature errors. Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 20-25, 30-33 rejected under 35 U.S.C. 102(e) as being anticipated by Marino et al. (WO 2005/097111, published October 20, 2005, filed March 22, 2005, claiming priority back to 60/561,188, filed 9 April 2004). Claims 20-24 and 31 are anticipated by Marino et al. because they teach the elected species, 2-(1-cyclopentylpiperidine-4-yloxy)-5-(4-cyanophenyl)pyrimidine (see page 6, line 14). The elected species has the following meaning for each variable: Y is 4-cyanophenyl; X_1 and X_2 are N; X_3 is C; W is formula II where m=1; and R is cyclopentyl. Claim 32 is anticipated because Marino et al. also discuss the use of pharmaceutically acceptable salts of the compound prepared in medicinal applications. Some of the salts listed (page 8, line 26 to page 9, line 8) as pharmaceutically acceptable include acetate,

benzenesulfonate, benzoate, bicarbonate, bisulfate, etc. Claim 33 is anticipated because Marino et al. are using the compound to treat movement disorders, including disorders such as Parkinson's disease, tremor associated with craniofacial trauma, etc. (see page 14, claims 4-9).

5. Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 33 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The issues concerning the meanings of "diabetes", "a circulatory system disease", "a disease accompanied by a sleep disorder", "electrolyte metabolism disorder", "emotional disorder", and "motion disorder", are discussed in the 35 U.S.C. 112, paragraph 2 rejection. Claim 33 does not describe the all of the diseases in detail.

According to the MPEP §2163 I. A. "the issue of a lack of adequate written description may arise even for an original claim when an aspect of the claimed invention has not been described with sufficient particularity such that one skilled in the art would recognize that the applicant had possession of the claimed invention. The claimed invention as a whole may not be adequately described if the claims require an essential or critical feature which is not adequately described in the specification and which is not conventional in the art or known to one of ordinary skill in the art." The MPEP states in §2163 II 3 ii)

"The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice (see i)(A), above), reduction to drawings (see i)(B), above), or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus (see i)(C), above). See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406."

According to the MPEP §2163.02 Standard for Determining Compliance With the Written Description Requirement, "The courts have described the essential question to be addressed in a description requirement issue in a variety of ways. An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed". In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). Under Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed. The test for sufficiency of support in a parent application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter". Ralston Purina Co. v. Far-Mar-Co., Inc., 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985) (quoting In re Kaslow, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983))."

This case was filed before Applicants had a clear idea of the diseases to be treated with these compounds. The specification provides broad areas of future research and speculation, inviting undue experimentation in learning how to use Applicants' invention.

Applicants are reminded of what the U.S. Court of Appeals Federal Circuit wrote in University of California v. Eli Lilly and Co. 43 USPQ2d 1398, "In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus." "A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See Fiers, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (discussing Amgen). "It is only a definition of a useful result rather than a definition of what achieves that result." "The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.")".

7. Claim 33 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the preparation of compounds 1-74, does not reasonably provide enablement for the ability of all of these compounds to inhibit the histamine H3 receptor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Applicants show how compounds 1-74 can be prepared on pages 73-97, as well as the testing of compounds 1, 11, 23, 37, 60, 65, and 68 on page 64. The IC_{50} (nM) of each compound tested is shown. This compounds tested cannot be considered representative of all of the compounds prepared because examples 1, 11, 23, 37, 60 have X_1 and X_2 as Nitrogen and variable Y as phenyl or 1,2,4-triazolo[4,3-a]pyridine. Examples 65 and 68 show X_1 or X_2 as N (but not both) and a 1-methyl-1H-pyridin-2on-5-yl

ring as Y. These compounds are not representative of all the envisaged compounds of claim 20 because Q_1 can be an alkyl group or any cyclic group.

> The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

(1) The nature of the invention and (2) the breadth of the claims:

The claims are drawn to compounds of formula I that can treat various disorders through modulation of the histamine H3 receptor. Thus, the claims taken together with the specification imply that every compound encompassed in claim 20 will treat the disorders listed in claim 33.

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

The compounds of claim 20-31 are known in the art.

Based upon analysis of data provided by applicants on page 64, inhibitors of the H3 receptor follow two trends: one, compounds with an electron-withdrawing group on the phenyl ring (variable Y when Q_1 is a 6-membered aryl ring) at the para position (compounds 1, 11, 23, 37, and 60) can inhibit H3 receptors; and two, compounds 65 and 68 show that when variable R is electron-donating, and compounds with an electron-donating group as variable R will inhibit the H3 receptor. Compounds with groups with the same properties (electron withdrawing for 1, 11, 37, and 60) and electron-donating groups (example 65 and 68) as variable R function as H3 receptor inhibitors.

(5) The relative skill of those in the art:

One of ordinary skill in the art is a chemist who is skilled in the use of protecting groups in organic synthesis.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided guidance for preparation of compounds 1-74 and testing of compounds 1, 11, 23, 37, 60, 65, and 68 against histamine H3 receptors.

However, the specification does not provide guidance that all of the compound encompassed by claim 20 can modulate H3 receptors. Only a limited scope of the compounds is shown to actually have an IC_{50} in low nanomolar amounts against the receptor.

Applicants are not enabled for the prevention of Alzheimer's disease. Pulley et al. (US 7,067,507, published June 27, 2006) state: "At present there are no effective treatments for halting, preventing, or reversing the progression of Alzheimer's disease" (column 2, lines 40-42).

Applicants are not enabled for the treatment of attention deficit hyperactivity disorder (ADHD). Fox et al. (*Behavioural Brain Research*, **2002**, *131*, 151-161) state "it is possible that ciproxifan may be augmenting dopamine release indirectly through blockade of H3 presynaptic receptors." Fox et al. also state "It is also possible that simultaneous modulation of H3 autoreceptors and heteroreceptors may indirectly increase release of neurotransmitters such as dopamine ..., leading to the improved blockade observed in this and other studies. However, since microanatomical differences have recently been noted in the adult (4-6 months) SHR hippocampus, we cannot exclude the possibility that the strain-related behavioral differences observed might be due to differential hippocampal development ..." (page 159, paragraph 1). Therefore, modulation of the H3 receptor may not necessarily treat ADHD.

(8) The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above, particularly with regards to the lack of novelty of the elected species and the high unpredictability in the art as evidenced therein, and

the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claim 33 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply.

1. The term "a circulatory system disease" is unclear. Even though several cardiovascular diseases are listed, the term is much broader than the specific diseases cited. Does the term refer to infections (such as bacterial endocartitis), pregnancy complications, or vascular diseases, for example? ("MeSH result", http://www.ncbi.nlm.nih.gov/sites/entrez?Db=mesh&Cmd=ShowDetailView&TermToSearch=68002318&ordinalpos=3&itool=EntrezSystem2.PEntrez.Mesh.Mesh_ResultsPanel.Mesh_RVFull, accessed June 27, 2007.)

2. The term "electrolyte metabolism disorder" is unclear because it encompasses several diseases, including dehydration, hypercalcemia, hyperkalemia, etc. There is no guidance in the specification for what is meant by this term. ("Water-Electrolyte Imbalance", http://www.nlm.nih.gov/cgi/mesh/2007/MB_cgi?mode=&term=Water-Electrolyte+Imbalance&field=entry, accessed June 28, 2007.)

3. "Diabetes" is unclear. What type is of diabetes is being treated, diabetes mellitus or insipidus? Diabetes mellitus is an endocrine system disorder and diabetes insipidus is a pituitary disease. ("Pituitary Diseases", http://www.nlm.nih.gov/cgi/mesh/2007/MB_cgi?mode=&term=Pituitary+Diseases&field=entry#TreeC19.700, accessed June 28, 2007.)

5. "Emotional disorders" is unclear. There is no guidance to what is meant by this term. In addition, this term can be interpreted as depression, post-traumatic stress disorder, phobias, or anxiety, for example. This term is vague and there is no guidance for what is meant by this term in the specification.

6. The phrase "A disease accompanied by a sleep disorder" is unclear because it can be interpreted as *any* disease (including any cardiovascular disease, for example) that is present in the patient along with a sleep disorder. The "disease" can be any ailment, and is therefore unclear.

7. "Motion disorder" is unclear. Motion disorders can be in three areas, cumulative trauma disorders ('Cumulative Trauma Disorders", http://www.nlm.nih.gov/cgi/mesh/2007/MB_cgi?mode=&index=11628&field=all&HM=&II=&PA=&form=&input=, accessed June 27, 2007.), Motion sickness ("Motion Sickness", http://www.nlm.nih.gov/cgi/mesh/2007/MB_cgi, accessed June 27, 2007.), and neurologic disorders ("Gait Disorders, Neurologic", http://www.nlm.nih.gov/cgi/mesh/2007/MB_cgi?mode=&index=18843&field=all&HM=&II=&PA=&form=&input=, accessed June 27, 2007.). Since this term can be interpreted at least three different ways, it is unclear.

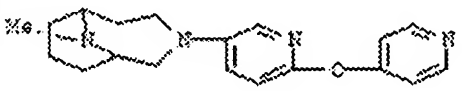
Allowable Subject Matter

10. No claims are allowed.

11. Claims 26-29 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

12. The following is a statement of reasons for the indication of allowable subject matter: The closest prior art of record is the following structure:

IN 9,10-Diazabicyclo[4.3.1]decane, 10-methyl-3-(6-(4-pyridinyloxy)-3-pyridinyl)- (9CI)
MF C19 H24 N4 O



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

This structure does not read on the claims because W cannot be a pyridine ring.

Conclusions

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Noble Jarrell whose telephone number is (571) 272-9077. The examiner can normally be reached on Monday-Friday from 7:30 to 6:00. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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